

In each of claims 42 and 43, insert
--eukaryotic--after "host".

R E M A R K S

The present invention provides biologically active, heterodimeric hormones (i.e., hormones containing an alpha and a beta subunit, which are encoded in nature by distinct mRNA's) in a single cell, either containing two vectors, one encoding the alpha subunit and the other encoding the beta subunit, or one vector encoding both. The inventors found that, even though the cells in which the two-subunit hormones are produced are undifferentiated cells, unlike the highly specialized cells which produce the hormones in the human body, post-translational heterodimer assembly occurs intracellularly to produce a biologically active hormone. The production of both subunits in one cell carries with it the advantage of the elimination of the need to combine the subunits after synthesis. This result was unexpected, and is not suggested in any prior art of which applicants are aware.

The claims have been rejected under 35 U.S.C. §§112, 102, 103.

The rejection of claims 1 and 3 under §102 is met by the cancellation of claims 1 and 3.

The remaining claims were rejected over the prior art previously of record, in combination with newly-cited Pierce et al. The references other than Pierce et al. are not discussed

herein, having been discussed in the previous response, which discussion is hereby incorporated by reference.

Regarding Pierce et al., the Examiner's attention is directed to the accompanying Declaration of John G. Pierce, the author of the Pierce et al. reference. As is explained in detail in the Pierce declaration, the in vitro association work mentioned in the Pierce et al. paper in no way renders obvious applicants' discovery that the two subunits of a hormone could be synthesized and made to associate to form an active hormone in a cell not specialized to make the hormone.

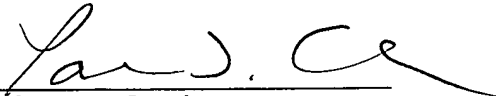
Turning now to the remaining grounds for rejection, a substitute Declaration of Availability will be submitted in due course, as will an appropriate terminal disclaimer meeting the obviousness-type double patenting rejection.

Regarding the overbreadth rejection, applicants agree with the Examiner that microbial hosts, which cannot glycosylate proteins, should be excluded; the present amendment requires that the cells be eukaryotic (support: specification, p. 1, line 24). Because it is well-known that eukaryotic cells other than mammalian cells (for example, other vertebrate cells) are capable of glycosylating proteins, it is believed that "mammalian" would be unnecessarily narrowing.

The typographical error in claim 33 has been corrected, and claim 34 has been cancelled.

In view of the above, it is submitted that all of the claims in the application are now in condition for allowance, and such action is requested.

Respectfully Submitted,



Paul T. Clark
Attorney for Applicants

Fish & Richardson
One Financial Center
Boston, MA 02111
Tel.: (617) 542-5070